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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,240	03/23/2005	Stefan Wildt	GFI-102	3290

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EXAMINER	
HAMA, JOANNE	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,240	WILDT ET AL.	
	Examiner	Art Unit	
	JOANNE HAMA	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-12,14,15,17,59 and 66-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-12,14,15,17,59 and 66-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of "galactosyltransferase" (see claims 7, 71, 83) of a specific transferase and "UDP-GlcNAc transporter" (see claims 70, 82) of a sugar transporter in the reply filed on June 3, 2010 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

With regard to the election of species use of a wild type or fusion proteins of alpha-1,2 mannosidase and GnTI, Applicant indicates that the claims have been amended to fusion proteins of alpha-1,2 mannosidase and GnTI (Applicant's response, page 9).

As a reminder to the species election of November 11, 2006, Applicant elected Pichia pastoris (see claim 17).

In the claim amendment filed March 11, 2010, claims 4, 5, 13, 16, 18-58, 60-65 were cancelled. Claims 1-3, 6, 7, 17, 59, were amended. Claims 66-88 were new.

In the claim amendment filed June 28, 2010, claims 4, 5, 13, 16, 18-58, 60-65 are cancelled. Claims 1-3, 6 are amended.

Claims 1-3, 6-12, 14, 15, 17, 59, 66-88, drawn to a method for producing a recombinant glycoprotein in a unicellular or filamentous fungi, are under consideration.

It is noted that Applicant has submitted a response to the Non-Final Action of September 24, 2009 on March 11, 2010.

Information Disclosure Statement

Applicant filed Information Disclosure Statements on March 11, 2010 and August 6, 2010. The IDSes have been considered. It is noted that in the IDS filed March 11, 2010, that reference 2, Maras et al., 1999, has been lined through and indicated as a duplicate ("dup") as it has been previously cited in the IDS of November 8, 2005.

Withdrawn Rejections

35 USC § 112, 1st parag., Written Description

Applicant's arguments, see pages 9-11 of Applicant's response, filed March 11, 2010, with respect to the rejection of claims 1-3, 6-12, 14, 15, 59 have been fully considered and are persuasive. Applicant refers to Figures 1 and 2 of the specification and indicates that in Figure 2 of the specification, Alg3 attaches the mannose to the 1,6 arm in an alpha-1,3 linkage and that the name of the enzyme refers to the sugar linkage catalyzed by the enzyme and not to the arm of the lipid-linked oligosaccharide it puts the sugar on (Applicant's response, page 9). The rejection of claims 1-3, 6-12, 14, 15, 59 has been withdrawn.

35 USC § 112, 2nd parag.

Applicant's arguments, see page 11 of Applicant's response, filed March 11, 2010, with respect to the rejection of claims 8, 9 have been fully considered and are persuasive. Applicant indicates that as indicated in the response to the Written Description rejection, the Alg3p enzyme transfers a mannose residue to the 1,6 arm of

the lipid-linked oligosaccharide (Applicant's response, page 11). The rejection of claims 8, 9 has been withdrawn.

35 USC § 103

Applicant's arguments, see pages 11-14 of Applicant's response, filed March 11, 2010, with respect to the rejection of claims 1-3, 6, 7, 10-12, 14, 15, 17, 19, 59 as being unpatentable over Goss et al., 1995, Clinical Cancer Research, 1: 935-944, Yoshida WO 00/34490, published June 15, 2000, Gemmill et al., 1999, Biochimica et Biophysica Acta, 1426: 227-237, Burda et al., 1999a, Biochimica et Biophysica Acta, 1426: 239-257, Karaoglu et al., 2001, Biochemistry, 40: 12193-12206, Burda et al., 1999b, Glycobiology, 9: 617-625, Tremblay et al., 1998, Glycobiology, 8: 585-595, Sarkar et al., 1991, PNAS, USA, 88: 234-238, Moremen et al., 1991, The Journal of Cell Biology, 115: 1521-1534.have been fully considered and are persuasive. Applicant amended claim 1 such that the yeast comprise a transgene construct that expresses a recombinant glycoprotein (claim amendments, March 11, 2010). The combined references do not teach the introduction of a transgene construct that expresses a recombinant protein. The rejection of claims 1-3, 6, 7, 10-12, 14, 15, 17, 19, 59 has been withdrawn.

New Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 6-12, 14, 15 17, 59, 66-88 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Nakanishi-Shindo et al., 1993, The Journal of Biological Chemistry, 368: 26338-26345, see IDS November 8, 2005 in view of Roy et al., 2000, Biotechnol. Bioprocess Eng. 5: 219-226, Contreras et al., US Patent 6,803,225, patented October 12, 2004, Lin et al., 1985, PNAS, USA, 82: 7580-7584.

Nakanishi-Shindo et al. teach Saccharomyces cerevisiae that comprise mutations in och1, mnn1, and alg3. Nakanishi-Shindo et al. teach that the Δoch1 mmn1 alg3 mutants accumulated Man5GlcNAc2 and Man8GlcNac2 in total cell mannoprotein, confirming the lack of outer chain addition to the incomplete corelike oligosaccharide. Nakanishi et al. teach that Man8GlcNAc2 produced by these mutant yeast suggests a potential use for the yeast as a host cell to produce glycoproteins contaiing mammalian high mannose type oligosaccharides (Nakanishi-Shindo et al., abstract).

While Nakanishi-Shindo et al. yeast that lacks alpha-1,6-mannlsyltransferase (och1) and lacks an enzyme that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide (alg3), they do not teach nucleic acids encoding i) an alpha-1,2 mannosidase catalytic domain fused to a targeting peptide that targets the ER or Golgi, ii) a GlcNAc transferase I (GnT I) catalytic domain fused to a peptide that targets the ER or the Golgi, and iii) a recombinant glycoprotein.

With regard to the claims being drawn to the expression of alpha 1,2-mannosidase and GnT-1 (claim 1), at the time of filing, Roy et al. teach that the HDEL

(His-Asp-Glu-Leu) sequence acts as a retention/retrieval signal for the ER. Roy et al. teach that HDEL was fused to the C-terminal of A. saitoi alpha-1,2-mannosidase and expressed in yeast and that the alpha-1,2-mannosidase converted Asn-linked Man8GlcNAc2 oligosaccharides into Man5GlcNAc2, the intermediate where mammalian-type sugar chains and S. cerevisiae sugar chains are identical (Roy et al., page 221, 1st col., 3rd parag.; page 222, 2nd col.). Roy et al. teach that the next step of building N-linked oligosaccharides is to add GlcNAc residues in the Golgi apparatus. To make this possible, the N-acetylglucosaminyltransferase (GnT-1) and UDP-GlcNAc transporter are necessary to be introduced into the yeast. Roy et al. teach that the rat GnT-1 was successfully expressed in various organelles, but most of it was in the Golgi apparatus. While Roy et al. do not specifically teach that the catalytic domains of enzymes were used, the art teaches that it is routine to use the catalytic domains of glycosylation enzymes and that they can be targeted to the ER. For example, Contreras et al. teach that fragments of alpha1,2-mannosidase can be fused to a ER retention signal such as HDEL (Contreras et al., col. 2, 4th parag. under Summary of the Invention). With regard to obtaining fragments, Contreras et al. teach that those in the art can readily identify and make functional parts of an enzyme based on analysis of the protein sequence (Contreras et al., col. 9, 6th parag.).

With regard to the claims being drawn to a UDP-GlcNAc transporter (claims 70, 82), Roy et al. teach that a UDP-GlcNAc transporter from K. lactis and human (Roy et al., page 223, 1st. col., 1st and 2nd parags.) can be expressed in yeast and that they localize to the Golgi and ER. With regard to the expression of mannosidase II (claims 2,

67, 80), which will trim GlcNAcMan5GlcNAc2 to GlcNAcMan3GlcNAc2, Roy et al. teach that human UDP-N-acetylglucosamine (alpha-6-D-mannoside-beta-1,2-N-acetylglucosaminyltransferase II was used (Roy et al., page 223, 2nd col., 1st parag.). With regard to the use of GnT-II (claims 3, 4, 68, 69, 81), Roy et al. teach that the successful addition of GlcNAc to GlcNacMan3GlcNAc2 serves as an acceptor for the galactose addition. With regard to the expression of galactosyltransferase (claims 7, 71, 83), human beta-1, 4-galactosyltransferase in was expressed in S. cerevisiae and has been shown to localize to the Golgi and have activity. With regard to the claims being drawn to the glycoprotein comprises sialic acid (NeuNAc) (claims 14, 15, 76, 77. 86, 87), Roy et al. teach that sialic acid can be added by in vitro enzymatic reaction after the successful synthesis of asialoglycoproteins (Roy et al., page 224, 1st col., 1st parag.).

With regard to the claims being drawn to the reaction including a nucleic acid sequence encoding a recombinant glycoprotein (claim 1), Roy et al. teach that therapeutic glycoproteins are of interest and one such glycoprotein that can be glycosylated in yeast is erythropoietin (EPO) (Roy et al., page 220, under Therapeutic Glycoprotein). As such, an artisan would have included an expression vector comprising the sequence of EPO to the recombinant yeast described by Roy et al. It is noted that the sequence for human EPO was known at the time of filing, see Lin et al., Figure 3.

With regard to the host bell being Pichia pastoris (claims 17, 78, 79 88), Roy et al. teach that Pichia pastoris has been used as a host to make recombinant glycoproteins (Roy et al., page 221, 1st col., 1st parag.).

Thus, the claims are rejected.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-

272-2911. The examiner can normally be reached Mondays, Wednesdays, Thursdays, and Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Joanne Hama/
Primary Examiner
Art Unit 1632